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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MCELWAIN, ELIZABETH F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 07/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,772	FEUSSNER ET AL.	
	Examiner	Art Unit	
	Elizabeth F. McElwain	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20 and 22* is/are pending in the application.

4a) Of the above claim(s) *2,3,15-18,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1 and 4-14 in the reply filed on May 14, 2004 is acknowledged. The traversal is on the ground(s) that Example 17 of Annex B of the PCT Administrative Instructions sets forth that unity of invention exists between a protein and a DNA sequence encoding that protein, so that Groups I and II should be rejoined. In addition, applicant argues that Group III is drawn to a fatty acid prepared by the method of claim 9, which is part of Group I. Furthermore, applicant asserts that Group IV is directed to using a nucleic acid sequence of Group I and should be rejoined. This is not found persuasive because in the present claims there is no one-to-one correlation between the DNA and the protein. The present claims are drawn to a genus of sequences, as stated in the restriction requirement. Furthermore, in Group I there are claims drawn to a first product, a first method of making, and a first method of using said product. The examination of additional products and methods is not required.

The requirement is still deemed proper and is therefore made FINAL.

The amendment filed May 14, 2004 has been entered.

Claims 2 and 3 are newly amended.

Please note that the renumbering of the claims in the last office action was in error, given that applicants had cancelled claims 19 and 21. Therefore, claims that are presently numbered 19 and 20 have been returned to the original numbering as claims 20 and 22, and that subsequent amendments should refer to claims 19 and 21 as cancelled claims.

Specification

2. The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. New application papers with lines double spaced on good quality paper are required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The specification is objected to given that there is currently no Brief Description of the Drawings.

The specification is objected to for failure to provide any headings, as set forth above.

The specification is also objected to for failure to comply with the sequence rules which require that all sequences be identified by a SEQ ID number. However, the sequences provided in Figure 2 are not identified by SEQ ID number either in the figure or in the specification. Correction is required. A new CRF, a new paper copy of the sequence listing, and a letter stating that the CRF and the paper copy are the same, are each required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6 and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to organisms, including animals, which includes humans; wherein humans are non-statutory subject matter.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 4-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, and all claims dependent thereon, are indefinite in the recitation of "amino acid sequences shown in SEQ ID NO: 2", since use of the plural sequences makes it unclear whether this refers to SEQ ID NO: 2 in it's entirety or if it refers to any portion of SEQ ID NO: 2. Amendment of the claim to recite the singular "sequence" would overcome the rejection.

Claim 1, and all claims dependent thereon, are indefinite in the recitation of "without substantially reducing the enzymatic activity of the polypeptides", since it is unclear what the metes and bounds of "substantially reducing" would be, and "reducing" is a relative term. However, no basis of comparison has been set forth. And the specification fails to define or clarify the use of this phrase.

Claims 4, 5, 7, 8, 13 and 14 for the recitation of "a" or "an" when referring to the product or method of a previous claim. Amendment of each of the claims to recite "the . . . as claimed in claim . . ." at each instance, would overcome the rejection.

Claims 4, 5, 6 and 8-12, and all claims dependent thereon, are indefinite in the recitation of "regulatory signals" with regard to nucleic acids, since this is not art recognized terminology. The amendment of the claims to recite "regulatory sequences" would overcome the rejection.

Claims 6, 9, 10, 11 and 12, and all claims dependent thereon, are indefinite in the recitation of "at least one" with regard to nucleic acids of claim 1, as it is unclear if the claim

is drawn to multiples of the same sequence from claim 1, or of any of the different sequences claimed in claim one, or if it is drawn to one of the sequences of claim one along with any other sequence that is not specified. Furthermore, there is no antecedent basis for more than one sequence of claim 1, as claim 1 is drawn to one nucleic acid sequence that is selected from the group set forth in the claim.

Claims 8 and 12 recite the limitation "functional or nonfunctional nucleic acid sequence" and "at least one nonfunctional nucleic acid sequence" in reference to claim 1. There is insufficient antecedent basis for this limitation in the claim. Furthermore, it is unclear what is intended by "functional" and "nonfunctional", since no particular function is specified.

Claim 9 is indefinite in the recitation of "oil-producing" organism, given that the Examiner is unaware of any organisms that do not produce some form of oil. Therefore, it is unclear what is intended.

6. Claims 1 and 4-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to nucleic acids that encode amino acid sequences having at least 75% homology to SEQ ID NO: 2 at the amino acid level, and has desaturase activity. However, the specification does not set forth what structural features of the amino acid sequence would be required to provide the functional activity of a desaturase. The specification only sets forth the desaturase of SEQ ID NO: 2.

"A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." In addition, "The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA . . . Accordingly, the specification does not provide a written description of the invention". See *University of California v. Eli Lilly and Co.,* 119 F. 3d 1559; 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997).

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

7. Claims 1 and 4-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding the calendulic acid desaturase of SEQ ID NO: 2, and expression of said enzyme in yeast, does not reasonably provide enablement for any desaturase coding sequence that codes for a protein having at least 75% homology to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Sequence homology is not sufficient to predict function of encoded sequences. See the teachings of Doerks (TIG 14, no. 6: 248-250, June 1998), where it states that computer

analysis of genome sequences is flawed, and "overpredictions are common because the highest scoring database protein does not necessarily share the same or even similar functions" (the last sentence of the first paragraph of page 248). Doerks also teaches homologs that did not have the same catalytic activity because active site residues were not conserved (page 248, the first sentence of the last paragraph). In addition, Smith et al (Nature Biotechnology 15:1222-1223, November 1997) teach that "there are numerous cases in which proteins of very different functions are homologous" (page 1222, the first sentence of the last paragraph). Also, Brenner (TIG 15, 4:132-133, April 1999) discusses the problem of inferring function from homology, stating that "most homologs must have different molecular and cellular functions" (see the second full paragraph of the second column of page 132, for example). Furthermore, Borks (TIG 12, 10:425-427, October 1996) teaches numerous problems with the sequence databases that can result in the misinterpretation of sequence data.

More specifically, identification of related sequences that will encode enzymes having a particular activity is particularly problematic in the enzymes involved in modifying fatty acids, and cannot be determined merely by similarity of DNA or amino acid sequences. Van de Loo et al teach that sequences encoding fatty acid hydroxylase activity are highly similar to other sequences that do not encode a hydroxylase, but instead encode a fatty acyl desaturase (see the abstract, at least). In fact, Broun et al teach that a change in only four amino acids will convert a desaturase gene to a hydroxylase gene (see the abstract, at least). Thus, if sequences are identified only by similarity to other sequences, one cannot conclude that these other sequences also encode an enzyme having the same activity. In fact WO 97/37033 (in IDS) and WO 98/46762 (in IDS) teach sequences that are at least 75% homologous to SEQ ID NO: 2,

yet encode enzymes with the wholly different activities of delta-12 acetylenase and delta-12 epoxygenase. Thus, sequences that fall within the scope of the claims may encode activities other than desaturases. However, the specification does not teach how one would identify which sequences that are similar to SEQ ID NO: 2 would have the claimed desaturase activity.

In addition, De Luca teaches that modifying plant biosynthetic pathways by transforming plants with genes encoding enzymes involved in said pathway is highly unpredictable (see the paragraph bridging the columns on page 225N, for example), and that "on many occasions desired goals have been impossible to achieve" (see the last paragraph on page 228N). Therefore, both the identification of other genes encoding fatty acid desaturase that falls within the scope of the claims, and the modification of plant lipid composition by transforming a plant with said gene or a portion of said gene are highly unpredictable. Furthermore, the specification provides no guidance and no examples of transforming any animals with the claimed sequences.

Thus, given the unpredictability of identifying sequences that exhibit fatty acid desaturase activity and modifying the lipid composition of a plant, microorganism or animal; the lack of guidance in the specification for identifying and characterizing other similar sequences that exhibit fatty acid desaturase activity; the lack of working examples of fatty acid desaturase activity coding sequences and other organisms transformed therewith, and the lack of working examples of similar sequences that encode proteins having the same activity, and the lack of working examples and guidance regarding use of said genes to modify a fatty acid; and given the breadth of the claims which encompass any sequence that codes for a protein that is at least 75% homologous to SEQ ID NO: 2, and transformed into any organism; and given

the state of the art which teaches similar sequences that have different enzyme activities; it would require undue experimentation by one skilled in the art to make and use the invention as broadly claimed.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1 and 4-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Hitz (US Patent 5,846,784).

The claims are drawn to a nucleic acid coding for a desaturase that has at least 75% homology to SEQ ID NO: 2, and said nucleic acid cloned into a vector and transformed into an organism, including a plant or a microorganism, and methods comprising transforming an organism.

Hitz teaches a nucleic acid coding for a desaturase that has at least 75% homology to SEQ ID NO: 2, and said nucleic acid cloned into a vector and transformed into an organism, including a plant or a microorganism, and methods comprising transforming an organism and extracting oil or fatty acids from said organism. Hitz teaches SEQ ID NO: 4 (columns 29-32) that has a 77.1% query match to SEQ ID NO: 2. Hitz teaches sequences encoding desaturase and epoxidizing enzymes and said sequences transformed into plants and microorganisms (col. 3, lines 15-19 and cols. 15-20). Furthermore, some amino acid sequences comprised in SEQ

ID NO: 2 would be found in any coding sequence, including that of the desaturase taught by Hitz.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1 and 4-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeBonte et al (US Patent 5,850,026), and further in view of Hitz (US Patent 5,846,784).

The claims are drawn to a nucleic acid coding for a desaturase that has at least 75% homology to SEQ ID NO: 2, and said nucleic acid cloned into a vector and transformed into an

organism, including a plant or a microorganism, and methods comprising transforming an organism and extracting oil or fatty acids from said organism.

DeBonte et al teach transforming a plant with a desaturase coding sequence for modifying the fatty acid composition of a plant, and extracting the fatty acids from the plant (see Examples 1 and 2, at least).

DeBonte et al do not teach a nucleic acid coding for a desaturase that has at least 75% homology to SEQ ID NO: 2.

Hitz teaches a nucleic acid coding for a desaturase that has at least 75% homology to SEQ ID NO: 2, and said nucleic acid cloned into a vector and transformed into an organism, including a plant or a microorganism, and methods comprising transforming an organism and extracting oil or fatty acids from said organism. Hitz teaches SEQ ID NO: 4 (columns 29-32) that has a 77.1% query match to SEQ ID NO: 2. Hitz teaches sequences encoding desaturase and epoxidizing enzymes and said sequences transformed into plants and microorganisms (col. 3, lines 15-19 and cols. 15-20). Furthermore, some amino acid sequences comprised in SEQ ID NO: 2 would be found in any coding sequence, including that of the desaturase taught by Hitz.

Given the recognition of one of ordinary skill in the art of the value of transforming an organism with a desaturase gene to modify the fatty acid composition of the organism, as taught by each of Hitz and DeBonte et al, it would have been obvious as a whole to one of ordinary skill in the art at the time the invention was made to transform a plant with a desaturase coding sequence and extract the fatty acids to evaluate plants form modified fatty acid composition, as taught by DeBonte et al, and it would have been obvious to substitute

another fatty acid modifying enzyme coding sequence, such as the sequence taught by Hitz. Thus the claimed invention would have been prima facie obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

Claim 13 is deemed free of the prior art given that increasing calendulic acid in an organism transformed with a desaturase coding sequence was not known or suggested in the prior art of record.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth F. McElwain whose telephone number is (571) 272-0802. The examiner can normally be reached on increased flex time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Elizabeth F. McElwain, Ph.D.
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Art Unit 1638

EFM